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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/462,682	04/28/2000	DAVID J. FITZGERALD	015280-31010	5396

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EXAMINER

PORTNER, VIRGINIA ALLEN

ART UNIT	PAPER NUMBER
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1645

DATE MAILED: 07/18/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/462,682

Applicant(s)

FITZGERALD, DAVID J.

Examiner

Ginny Portner

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 18 April 2005.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) 1-3, 7-8, 12-13 and 47-50 4-6, 11, 14-23, 26, 28, 31, 32, 34-36 and 39-43 is/are pending in the application.

4a) Of the above claim(s) 4-6, 11, 14-23, 26, 28, 31, 32, 34-36 and 39-43 is/are withdrawn from consideration.

- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-3, 7-8, 12-13 and 47-50 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

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DETAILED ACTION

Claims 1-3, 7-8, 12-13 and 47-50 are under consideration. All other claims stand withdrawn from consideration (4-6,11,14-23,26,28,31-32,34-36,39-43) or have been canceled (9-10,24-25,27,29-30,33,37-38,44-45 and 46).

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on April 18, 2005 has been entered.

Rejections Withdrawn

2. Claims 2, 7 and 8 are no longer objected to for not being further limiting of the claim from which they depend, in light of the amendments of claims 1 and 2.
3. Claims 1-3, 7-8,12-13, 46-50 rejected under 35 U.S.C. 103(a) as being unpatentable over Wels et al and Pastan et al is herein withdrawn in light of the newly entered combination of claim limitations and traversal set forth in Applicant's remarks.

Rejections Maintained

4. Claims 1-3, 7-8, 12-13 and 47-50 are rejected under 35 USC 112,first paragraph written description, as previously applied to claims 1 and 47, is herein maintained for reasons of record and responses set forth below under ***Response to Arguments***.

Response to Arguments

5. The rejection of claims 1-3, 7-8, 12-13 and 47-50 as previously applied to claims 1 and 47 under 35 USC 112, first paragraph written description is traversed on the grounds that the instant Specification incorporates by reference, Siegall et al (1991, Biochemistry), which teaches amino acids 339 and 343 appear to necessary for translocation and that positions 341 and 344 can be mutated.

6. It is the position of the examiner that critical claim limitations that find support in a journal reference that is incorporated by reference is improper incorporation by reference to critical subject matter that is claimed. Additionally, the claims do not recite that positions 339, 343, 341 or 344 are the positions that are intended to be maintained or mutated as argued by Applicant. All positions may be mutated based upon the combination of claim limitations recited in the claims, as long as the sequence maintains 95% identity to the recited range of amino acids of SEQ Id NO 2. Applicant's arguments directed to positions that are not to be mutated verses specific positions that can be mutated are not commensurate in scope with the instantly claimed invention which may mutant any one or more positions within the recited range of amino acids of 280-344, as long as the number of mutations meets the recited percent identity of 95%.

7. A genus of polypeptide translocation domains of the recited degree of variation has not been disclosed, nor described in such a way that one of skill in the art would have known that Applicant was in possession of the claimed invention at the time of filing for the instant invention. The independent claim has been amended to define the recited range to be a subsequence of the polypeptide amino acid sequence for the translocation domain, and the overall amino acid sequence is not limited to sequences from

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Pseudomonas aeruginosa exotoxin A, amino acids 280-344. The combination of claim limitations has not been described, because the overall sequence of the polypeptide has only been defined by function and not structure, and while the subsequence portion is structurally defined with reference to a range of amino acids 280-344 of SEQ ID NO 2, the claimed genus of variants with any type of changes at any position within this range (280-344 of SEQ ID NO 344) has not been described, nor evidences original descriptive support, in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim Objections

8. Claim 47 is objected to because of the following informalities: Claim 47 depends from withdrawn claim 15 and therefore is unclear, and is not further limiting of the claim from which it depends as claim 15 is not under consideration. Appropriate correction is required.

Claim Rejections - 35 USC § 112

9. Claims 1, 3, 7, 12-13, 47-50 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 1, 3, 7, 12-13, 47-50 in subparagraph (2) recite a new combination of claim limitations: “a translocation domain comprising a polypeptide having an amino acid **subsequence** at least 95 % identical to the sequence of *Pseudomonas* exotoxin A (PE) (SEQ ID NO 2) from amino acid position 280 to amino acid position 344 thereof and wherein the domain is capable of effecting translocation to the cytosol of the cell”.

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While it is clear that the translocation domain must comprise a “subsequence” that shares least 95 % of the amino acids defined by the range 280-344 of SEQ ID NO 2, the overall structure of the translocation domain is not so limited to the recited range, because the range of amino acids that shares 95% with amino acids 280-344 of SEQ Id NO 2 is a “subsequence” within the translocation domain now claimed, and overall structure of the claimed translocation domain is only functionally define by the recitation of the phrase “capable of effecting translocation to the cytosol of the cell”. What the over all structure of the translocation domain is, is not distinctly claimed, as a biological function does not defines any specific combination of molecules or amino acids.

10. Claims 1-3,7-8,12-13,47-50 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1 has been amended to recite the phrase: “(3) an epitope presenting domain having an amino acid sequence of between 5 and 350 amino acids in length consisting essentially of one cysteine to cysteine disulfide bonded loop of a pathogen wherein the loop encodes an epitope of the pathogen”.

Paragraph (3) defines a domain to contain 5 to 350 amino acids, but redefines the domain to “consisting essentially of one cysteine to cysteine disulfide bonded loop”. This is only two amino acid, and not the minimum of 5 amino acids. Additionally, the loop encodes the epitope, but the loop comprises one cysteine-to-cysteine disulfide amino acid sequence. The proposed combination of claim limitations is not internally consistent with respect to the size and sequence of the epitope presenting domain. Clarification is requested.

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11. Claim 47 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 47 depends from a withdrawn claim (claim 15) and therefore does not clearly set forth the invention under consideration.

12. Claims 49-50 are rejected under 35 USC 112, second paragraph for reciting the limitation "the cell" in an effort to further limit the immunogen of claim 1, but claim 1 does not comprise a cell, but a cell recognition domain which is only a portion of a cell. A portion of a cell does not provide antecedent basis for an entire cell. There is insufficient antecedent basis for this limitation in claim 1 from which they depend. This rejection could be obviated by amending claims 49-50 to recite: -----cell recognition domain-----.

Claim Rejections - 35 USC § 102

13. Claims 1, 7-8, 12, 47-50 are rejected under 35 U.S.C. 102(e) as being anticipated by Cardy et al (US 2002/0106370, effective filing date May 15, 1995).

(Instant claims 1, 7-8, 12) Cardy et al disclose the instantly claimed invention directed to an immunogenic composition that comprises four functional domains, the domains being:

(1) a cell recognition domain (see Cardy et al page 3, paragraph [0014 "antibodies which bind to lymphocyte cell surface internalizing antigens"),

(2) a translocation domain (see Cardy et al page 8, claim 15 "the translocation domain of Pseudomonas exotoxin"),

(3) an epitope loop domain (see Cardy et al page 8, claim 12, "HIV-V3 loop epitope"),

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(4) endoplasmic reticulum retention domain (see Cardy et al, page 8, claim 13

“directing the peptide unit(s) to a particular cellular compartment”, see Figure 10,

“KDEL” a retention domain for the endoplasmic reticulum of a cell).

Instant claims 49- 50: wherein the cell recognition domain recognizes any eukaryotic receptors (see Cardy et al, page 1, [0005, line 3] and page 2, [0010 “human or animal subject”]).

Cardy et al inherently anticipates the instantly claimed invention because Pseudomonas exotoxin translation domain is domain II of the exotoxin and the amino acid sequence of the exotoxin is an inherent structural characteristic defined by Swiss-Prot accession number P11439. By all comparable data, the claimed composition of Cardy et al is the same or equivalent composition now claimed.

Conclusion

14. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

15. Pastan et al and Fitzgerald et al patents are cited to show various chimeric polypeptides, specifically US Pat. 6,011,002 is cited to show circular ligands that comprise disulfide bonds see (col. 5, lines 27-38) and Pastan et al (US Pat. 6,074,644 is cited to show the insertion of a heterologous polypeptide at the 1b domain location within Pseudomonas aeruginosa exotoxin A(see figure 1).

16. US Pat. 5,612,036 is cited to show a loop epitope of Pseudomonas pilin protein between two cysteine residues, linked to a toxin carrier protein (see claim 1, col. 10, lines 6-10; col. 8, lines 63-67).

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17. Cryz, Jr (1995) is cited to show a *Pseudomonas aeruginosa*-HIV V3 loop epitope chimera for induction of an immune response. Catasti et al (1995) is cited to show HIV V3 loop epitope is more immunogenic when held in a loop confirmation.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ginny Portner whose telephone number is (571) 272-0862. The examiner can normally be reached on M-F, alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (571) 272-0864.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Vgp
July 11, 2005


MARK NAVARRO
PRIMARY EXAMINER